

# Designing New Peptide as Inhibitors of OV-CAR-3 Cell Line

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**Abstract**— One of the significant oncogen proteins is Tropomyosin Related Kinase B (Trk B) which its ligand is Brain Derived Neurotrophic Factor (BDNF). Over-expression of Trk B was observed in thyroid, ovarian and prostate cancer and multiple myeloma. BDNF bind to Trk B receptor which leads to activation of angiogenesis and proliferation pathway in tumor cell line. The aim of this study was to design novel peptides as inhibitors of Trk B receptor. Firstly, peptide library was generated; bioinformatics software for opting peptides with lowest energy, then the designed peptides were treated on OV-CAR-3 Cell line. MTT Assay was carried out to investigate the cytotoxicity and apoptosis in OV-CAR-3 Cell line resulting from designed peptides. Our findings indicated that peptide II with 350 nM is more effective OV-CAR-3 than other designed peptides, it could inhibit signaling pathway.

**Keywords**— New peptide, Inhibitor, OV-CAR-3 cell line.

## I. INTRODUCTION

CANCER is the second cause of death in the world wild and Millions of people are suffering from cancer [1]. There are many ways for cancer treatment including surgery, radiation therapy, chemotherapy, targeted therapies like monoclonal antibody and therapeutic peptides [2]. The peptide has many advantages than others including smaller size, high structural compatibility with target proteins and fewer drug-drug interaction complications [3], [4]. Many proteins including RAS, WNT, MYC, ERK and TRK; So TRK have been identified as a drug target in cancer; Trk B receptor acts as an oncogen agent and its binding to BDNF ligand activates the signaling angiogenesis of tumor proliferation [5]. After binding BDNF to cytoplasmic Trk B receptor cause autophosphorylation Y484, Y785 activates some signaling including phosphatidylinositol 3-kinase (PI3K) active survival and growth, MAPK/ERK and RAS/MAPK differentiation and growth also AKT cause decreasing of pro apoptotic proteins [6],[7]. Trk B inhibition is potential target for treatment of some cancers [5, 8]

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because over expression and mutation in Trk B are determined in ovarian, bladder, neuroblastoma, prostate, multiple myeloma [9], [10]. In this study we set up a computational method for designing novel stable peptides for inhibition of Trk B as cell membrane receptor of BDNF.

## II. MATERIAL AND METHODS

We designed a peptide to disrupt its binding to BDNF and blocking the activation pathways of angiogenesis. At the first step, a peptide library generated. Then generated peptides sorted based on energy score in R package. Three dimensional Structures of the selective peptides with the lowest energy predicted by using molecular dynamic method in Hyperchem 7 software.

## III. RESULTS

Storing designed peptides and 3D- structure of them are shown in figure 1 and 2. MTT assay was done in 200 and 350 nM, IC50 of 200 and 350 nM was shown in figure 3. For OV-CAR-3 after the treatment of designed inhibitory peptide I at concentrations 200, 350, nM at 24h were 340.92 nM while for designed peptide II at concentration 200, 350 nM at 24h were 199.52, our result shown peptide II is more effective than peptide I (Figures I and II, Table I).

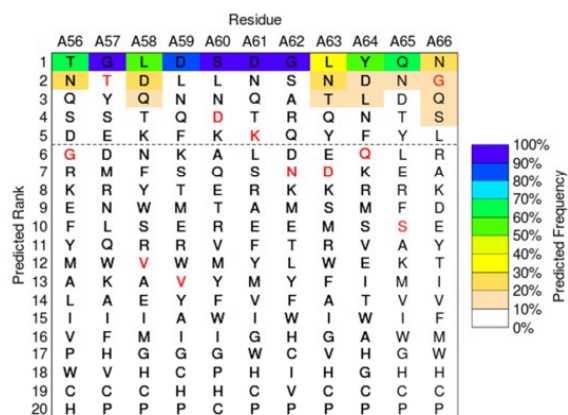


Fig.1 the five peptides with lowest energy is above of dot, are sorted by R package

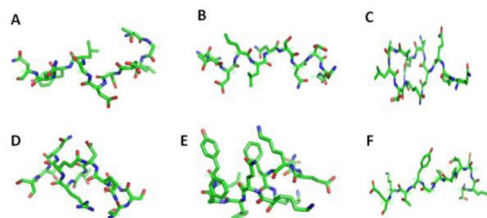


Fig. 2 three dimensional of designed peptides